ALTERATIONS IN AMPA RECEPTOR SUBUNIT IMMUNOREACTIVITY WITHIN THE HIPPOCAMPAL FORMATION OF BRAINS AFFECTED WITH ALZHEIMER'S DISEASE PATHOLOGY

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The role of the hippocampus in the process of learning and memory, as well as the importance of glutamate neurotransmission in that function have been well documented. In Alzheimer's disease (AD) it has been recognized that specific populations of neurons within the hippocampal formation are among those which are particularly susceptible to the pathologic insults of the disease. In considering possible mechanisms underlying the selective vulnerability of hippocampal neurons it is reasonable to propose that excitotoxicity specifically mediated via glutamate receptors participates in the pathological cascade associated with this disease. In our previous study we employed immunocytochemical techniques to determine in the hippocampal formation of aged human brain the distribution and anatomical features of those structures immunolabeled with antibodies directed against the AMPA-selective receptor subunits GluR1 and GluR2/3. In the present work we examined the alterations in the immunolabeling of these receptor subunits within the corresponding regions of age-matched cases diagnosed with Alzheimer's disease. In general the pattern of immunostaining in the AD cases was similar to that of controls. The most intense GluR1 immunoreactivity was observed in the molecular layer of dentate gyrus, while GluR2/3 staining was most prominent within the granular layer of dentate gyrus and the pyramidal layer of CA fields. Although a number of AD cases displayed a high degree of neurofibrillary pathology, largely restricted to the subiculum and CA1 field, the intensity of immunolabeling within the hippocampus of these AD brains appeared to be increased when compared to controls. Particularly there was an increase in GluR1 staining within the polymorphic layer of the dentate gyrus and in GluR2/3 labeling of pyramidal neurons in CA fields and the subiculum. Although the mechanism underlying these observations remains to be determined, we predict that in Alzheimer's disease alterations in glutamate receptor expression will alter the way a cell responds to glutamate and hence its vulnerability to glutamate excitotoxicity.